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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,301	01/22/2001	Michal Eisenbach-Schwartz	EISENBACH-SCHWARTZ=18	8567

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EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/765,301	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *2-7, 9, 11-19, 21, 23, 26-29, 32, 34-42, and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,10,20,22,24,25,30,31,33,43,44 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8,10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 13 May 2002 (Paper No. 9) has been entered in full. Claims 2, 4, 8-11, 21-25, and 27 are amended and claims 43-46 are added.

Election/Restrictions

Applicant's election of Group IV, claims 20-25 and 30-42, drawn to a method of treating injury or disease caused or exacerbated by glutamate toxicity comprising administering an effective amount of Cop 1 or a Cop 1-related peptide or polypeptide in Paper No. 9 (13 May 2002) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant argues that newly added claim 43 is a linking claim and therefore, all of the embodiments of claims 1-46 should be examined in this case once claim 43 has been found allowable. Although Applicant has not explained to the Examiner why any of the restricted groups should be rejoined to the elected Group IV, the Examiner has rejoined Groups I and IV.

The requirement is still deemed proper and is therefore made FINAL.

Claims 2-7, 9, 11-19, 21, 23, 26-29, 32, 34-42, and 45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9 (13 May 2002).

Claims 1, 8, 10, 20, 22, 24-25, 30-31, 33, 43-44, and 46 are under consideration in the instant application as they read upon the elected species of Cop 1, disease, and glaucoma.

Specification

1. The disclosure is objected to because of the following informalities:

(1a.) Patent applications are referenced in the disclosure (pg 55, line 12). The status of the applications must be updated.

(1b.) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "USE OF COPOLYMER-1 FOR INHIBITNG SECONDARY NEURONAL DEGENERATION IN GLAUCOMA".

Appropriate correction is required.

Claim Objections

2. Claims 1, 8, 10, 20, 22, 30-31, 33, 43-44, and 46 objected to because of the following informalities:

Claim 1, 8, 10, 20, 22, 30-31, 33, 43-44, and 46 recite non-elected species and groups.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 8, 10, 22, 24-25, 43-44, and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting secondary neuronal degeneration of ganglion cells caused or exacerbated by glutamate toxicity in the central nervous system (CNS) comprising administering to an individual with glaucoma an effective amount of

Cop-1 to inhibit secondary neuronal degeneration, does not reasonably provide enablement for a method for inhibiting neuronal degeneration caused or exacerbated by glutamate toxicity in the CNS of an individual in need thereof, comprising causing activated T cells, which have been activated by Cop-1, to accumulate at the site of neuronal degeneration in the individual in need. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims.

Claims 8, 10, 22, 24-25, 43-44, and 46 recite a method for inhibiting neuronal degeneration caused or exacerbated by glutamate toxicity in the CNS of an individual in need thereof, comprising causing activated T cells, which have been activated by Cop-1, to accumulate at the site of neuronal degeneration in the individual, with the proviso that the individual in need is other than one who has multiple sclerosis. The claims also recite that Cop-1 is administered in a manner which promotes active immunization of the individual so as to build up a critical T cell response. The claims disclose that the neuronal degeneration is a result of a disease.

The specification teaches that mice are subcutaneously administered Cop-1 emulsified in complete Fruend's adjuvant (CFA) or phosphate-buffered saline (PBS) in CFA. The mice are then subjected to sever crush injury in the intraorbital portion of the optic nerve (pg 71). Glutamate is injected into the right eye of the mouse and Fluorogold is injected into the superior colliculus of each hemisphere (pg 72). The specification discloses that immunization with Cop-1 results in a significant reduction in glutamate toxicity (pg 81, lines 1-2; Figure 8A-8C). The results also indicate that the protective efficacy of Cop-1 diminishes with the time between

immunization and glutamate insult (pg 81, lines 12-13). The specification also teaches that an increase in ocular pressure (IOP) is achieved in rats by laser photocoagulation of the limbal and episcleral veins (pg 76, lines 21-25; pg 77, lines 1-9). Rats are immunized with either Cop-1 emulsified in complete Freud's adjuvant (CFA) or phosphate buffered solution (PBS) on the day of the first laser treatment (pg 82, lines 17-21). After 3 weeks, retinal ganglion cells are retrogradely labeled (pg 82, lines 22-23). The specification discloses that the number of surviving retinal ganglion cells in the Cop-1 immunized rats is significantly higher than in the PBS injected controls (pg 83, lines 1-4; Figure 11A-C). The results also indicate that a slightly smaller effect is seen in rats that are immunized with Cop-1 when their IOP was already high (pg 83, lines 4-6; Figure 11D).

However, the specification does not teach inhibition of neuronal degeneration caused or exacerbated by glutamate toxicity in the CNS of an individual comprising causing activated T cells, which have been activated by Cop-1, to accumulate at the site of neuronal degeneration. Undue experimentation would be required of the skilled artisan to determine which cell types in the central nervous system are inhibited from neuronal degeneration. There are also no methods or working examples in the specification to indicate that primary neuronal degeneration (or the primary damage) is inhibited, as recited in the claims. A large quantity of experimentation would be required of the skilled artisan to inhibit primary neuronal degeneration of any cell type caused or exacerbated by glutamate toxicity. Furthermore, although the specification teaches that a large number of invading lymphocytes are observed in the vitreous 24 hours after glutamate injections (pg 91, lines 16-20), the skilled artisan would not be able to predict that those lymphocytes are activated by Cop-1 since other antigens, such as MBP, MOG, and β-

amyloid, may be present at the site of injury or disease in the central nervous system. There are also no methods or working examples in the instant application that indicate the invading lymphocytes are activated by Cop-1.

Due to the large quantity of experimentation necessary to determine which cells types are inhibited from neuronal degeneration, to inhibit primary neural degeneration of any cell, and to determine whether or not the T cells accumulating at the site or neuronal degeneration are activated by Cop-1, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, unpredictability of the effects of neuronal degeneration on T cell activation, and the breadth of the claims which fail to recite limitations as to the type of neural degeneration caused by glutamate toxicity as well as the cells affected, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 8, 10, 20, 22, 24-25, 30-31, 33, 43-44, and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Regarding claims 1, 8, 10, 20, 22, 24-25, 30-31, 33, 43-44, and 46, the acronym "Cop-1" renders the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

7. Claims 1 is indefinite because the claim does not have a step that clearly relates back to the preamble. For example, there is no step indicating that administration of Cop-1 protects cells from glutamate toxicity.

8. Claims 22, 24-25, and 43-44 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The administration of a compound, peptide, T cells, etc. to an individual to cause activated T cells to accumulate at the site of neuronal degeneration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (Neurology 45:1268-1276, 1995).

Johnson et al. teaches subcutaneous administration of copolymer-1 (Cop-1) to patients with remitting-relapsing multiple sclerosis (MS).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 20, 30-31, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (Neurology 45:1268-1276, 1995) in view of Pitt et al. (Nature Med 6(1): 67-70, 2000).

Johnson et al. teaches subcutaneous administration of copolymer-1 (Cop-1) to patients with remitting-relapsing multiple sclerosis (MS).

Johnson et al. does not teach that one of the contributing factors to multiple sclerosis is glutamate toxicity.

Pitt et al. teach that increased glutamate levels have been in the cerebrospinal fluid of patients with CNS inflammatory diseases, such as MS (pg 68, ¶ 2). Pitt et al. also disclose that during inflammation, glutamate is produced and released into the extracellular space by activated leukocytes and microglia. Pitt et al. further teach that an increase in extracellular glutamate, the main excitatory neurotransmitter in the CNS, can have potentially serious consequences, as it is capable of precipitating excitotoxic cell death (pg 68, ¶ 2).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to administer Cop-1 to individuals with multiple sclerosis as taught by Johnson et al. because glutamate toxicity is involved in the pathogenesis of MS, as taught by Pitt et al. The person of ordinary skill in the art would have been motivated to make that modification because MS is an inflammatory disease wherein the immune system attacks self molecules within the white matter of the brain and spinal cord and affects one million people world-wide. The person of ordinary skill in the art reasonably would have expected success because Cop-1 was already being administered to patients with multiple sclerosis at the time the invention was made. Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Osborne et al. Brit J Opthalmol 83: 980-986, 1999.

Steinman, L. Multiple approaches to multiple sclerosis. Nat Med 6(1): 15-16, 2000.

Hohlfeld, R. Phil Trans R. Soc Lond B 354: 1697-1710, 1999.

Goldblum et al. Vision Res 42: 471-478, 2002.

Kipnis et al. Proc Natl Acad Sci USA 97(13): 7446-7451, 2000.

Schori et al. Proc Natl Acad Sci 98(6): 3398-3403, 2001.

Schwartz, M. Drug Dev Res 50: 223-225, 2000.

Teitelbaum et al. Cell Molec Life Sci 53: 24-28, 1997.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BEB
Art Unit 1647
July 26, 2002

Gary L. Kunz

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